Pertussis:

What Washington State Health Care Providers Need to Know

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Introduction

Pertussis (whooping cough) is a highly communicable illness caused by *Bordetella pertussis* and *B. parapertussis*. This disease has a long history in North America. A pertussis outbreak apparently occurred in Plymouth colony in 1648, and pertussis was an almost universal childhood infection until a vaccine became available in the mid-1940s. Pertussis remains a public health problem in the United States despite the widespread use of vaccine. In 1984, King County experienced an outbreak of pertussis with 162 cases reported in a nine-month period. The previous year's annual average was only 40 reported cases for the entire state. In 1994, a total of 4,617 cases of pertussis were reported to the Centers for Disease Control and Prevention (CDC), representing only an estimated ten percent of the actual number of cases. During 1995–1996, several Washington state counties have reported outbreaks of pertussis including King County, Snohomish County, and Spokane County. In the United States, the mortality rate of pertussis is low, but the disease is severe in infants <6 months of age. The primary reservoir for pertussis is the adult population. Three factors contributing to this are:

a) waning of vaccine-induced or naturally acquired immunity among adolescents and adults who were vaccinated or infected as children

b) the often mild illness in older persons

c) the general perception that pertussis is an illness occurring only among children.

The primary objective of this monograph is to educate health care practitioners about pertussis in order to improve disease recognition, treatment, and reporting so that transmission of the disease can be limited through public health interventions.

“Whooping Cough cases on the rise

King County officials warn of potentially deadly disease

Adolescents and adults are usually the major carriers because vaccine-stimulated immunity fades over time.”

- Seattle Times, December 8, 1995

The Changing Epidemiology of Pertussis

in King County, Washington State

In the United States, pertussis incidence decreased from the 1940s, when the pertussis vaccine became widely available, until the mid-1970s. However, since then a general increase in incidence has occurred, including in Washington state (Figures 1 and 2). Pertussis is the only vaccine-preventable disease in which such a trend occurs.

A leading hypothesis for this trend is that natural, longer lasting immunity (which resulted from widespread childhood infection in the pre-vaccine era), has been replaced by <12 years of artificial immunity provided by the vaccine (see **Pertussis in Adults** and **Vaccines**). This may also explain a shift

Figure 1

Reported cases of pertussis per 100,000 by year in the United States, 1965–1994. The incidence has generally been increasing since the mid-1970s.

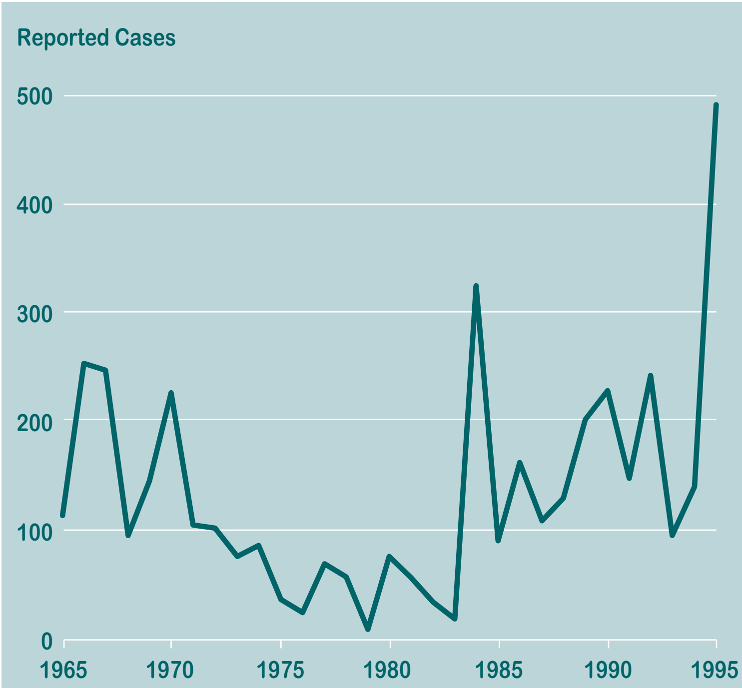

Figure 2

Reported cases of pertussis, by year in Washington state, 1965–1995. This figure presents cases reported to the state health department.

Age Group	Cases	Percent
< 7 mo	27	10.3
7 mo to 4 yrs	34	13.0
5 yrs to 17 yrs	96	36.6
≥ 18 yrs	105	40.1

Table 1

Age distribution of cases of pertussis in 1995, Seattle-King County pertussis outbreak.

to a greater proportion of cases occurring in adolescents and adults (in spite of their vaccination status).

King County has been experiencing an epidemic of pertussis which began in May 1995 and is still occurring. Data will be presented for 1995 only. This epidemic is the largest to have occurred in King County for >30 years. By December 31, 1995, a total of 262 cases among persons who had onset of disease during 1995 were reported to the health department and had been linked to the outbreak (an additional 250 cases with onset in 1996 were reported by November 30, 1996) (Figure 3). In most cases, pertussis was defined by the CDC case definition (Figure 4).

The age distribution of cases was remarkable for the number occurring in adolescents and adults (Table 1). Ten percent of cases occurred in young infants (i.e., children <7 months of age), 13% in preschool-age children (i.e., children 7 months–4 years of age), 37% in school-age children (i.e., children 5–17 years of age), and 40% in adults.

Laboratory confirmation by culture or direct fluorescent antibody (DFA) smear was most successful in infants (95%) and least successful in adults (29%) (Table 2). However, laboratory confirmation was rarely attempted for adults because recognition of their illness often occurred >3 weeks after their onset of symptoms. Serologic testing can be useful in diagnosis of cases recognized late, at least 2 weeks after onset. Thirty-six (14%) cases were considered laboratory confirmed based on serologic criteria.

Fifty-three clusters of cases were recognized in King County, ranging in size from two to 35 cases. Sites of exposure included the home (most often), school, and work sites. Index cases were identified in 44 clusters. In 21 (48%) of these clusters, the index case-patient was a school-age child or adolescent and, in another 21 (48%) clusters, the index case-patient was an adult. In the remaining two clusters, a young infant appeared to be the index case-patient.

The most critically ill case-patients were the 27 young infants. Although two-thirds of them were hospitalized (often in intensive care), none of the infants died. The likely source of infection for the young infants was an adult in 14 (52%) instances, a school-age child in five (19%) instances, and another infant in two (7%) instances. Either an infant was the only case-patient or the source was unknown in six (22%) instances.

Problems that were encountered during this epidemic included difficulty with the timing of specimen acquisition and interpretation of laboratory tests, late administration of and poor compliance with antibiotic prophylaxis, and failure to consider pertussis as a diagnosis for persons who had unexplained severe cough. Most of the adults who were eventually recognized as having pertussis presented to health care providers late in their illness. This made recovery of the organism less likely and led to

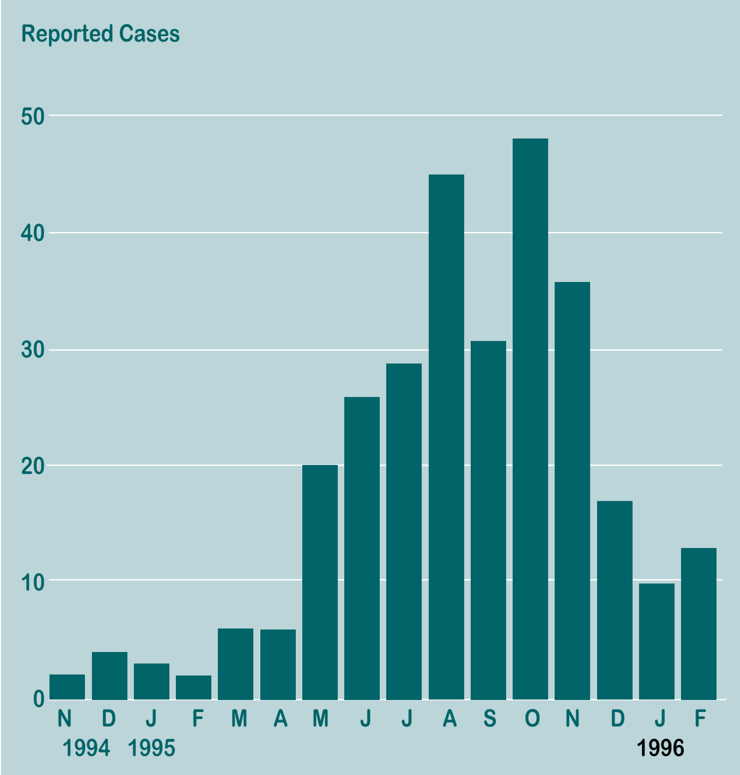

Figure 3

The 1995 pertussis epidemic, by month of onset in Seattle-King County.

Age group	Laboratory confirmed cases	Percentage of total in age group	Total
0–6 mo	19	95.0	20
7–12 mo	5	55.5	9
1–4 yrs	9	37.5	24
5–17 yrs	20	34.5	58
≥ 18 yrs	20	28.6	70

Table 2

Percentage of laboratory confirmed cases of pertussis by age in 1995, Seattle-King County pertussis outbreak.

Centers for Disease Control and Prevention case definition of pertussis (at the time of the 1995 King County pertussis outbreak).	**Case definition of pertussis approved by the Council of State and Territorial Epidemiologists in June 1996 (changes are in bold).**
Clinical case definition	**Clinical case definition**
A cough illness lasting at least 2 weeks with one of the following: paroxysms of coughing, inspiratory "whoop," or post-tussive vomiting, and without other apparent cause (as reported by a health professional).	A cough illness lasting at least 2 weeks with one of the following: paroxysms of coughing inspiratory "whoop," or post-tussive vomiting, and without other apparent cause (as reported by a health professional).
Laboratory criteria for diagnosis	**Laboratory criteria for diagnosis**
Isolation of *B. pertussis* from a clinical specimen.	Isolation of *B. pertussis* from a clinical specimen, or **Positive polymerase chain (PCR) reaction assay for** *B. pertussis*.
Case classification	**Case classification**
Probable. Meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory confirmed case. *Confirmed.* A clinically compatible case that is laboratory confirmed or epidemiologically linked to a laboratory confirmed case.	*Probable.* Meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory confirmed case. *Confirmed.* **A case that meets the clinical case definition** and is laboratory confirmed or epidemiologically linked to a laboratory confirmed case.

Comment. The clinical case definition should be used for endemic or sporadic cases. In outbreak settings, (five or more cases clustered in time and space), the clinical case definition used can be modified to "a cough illness lasting at least 2 weeks (as reported by a health professional)." Occasionally patients with an acute cough illness which lasts <14 days, but who are culture positive, are detected as part of household investigations; such cases may also be reported as confirmed cases of pertussis. Because direct fluorescent antibody testing of nasopharyngeal secretions has been shown in some studies to have low sensitivity and variable specificity, the Centers for Disease Control and Prevention does not recommend relying on this test for laboratory confirmation.

Figure 4
Definitions, laboratory criteria for diagnosis and case classifications.

reliance on epidemiologic information and serologic methods for case classification.

Antibiotic prophylaxis of all household and close contacts was difficult. Many case-patients were not diagnosed until after they had passed their most infectious phase of the disease such that antibiotic prophylaxis of their contacts would no longer be indicated. In addition, full compliance with two weeks of erythromycin prophylaxis at doses up to two grams each day was below 50%.

Finally, many health care providers did not consider pertussis as a diagnosis for persons of any age with otherwise unexplained severe cough. Frequently, adult patients and their health care providers expressed certainty that pertussis was not a likely diagnosis because of the patient's age and the absence of the characteristic "whooping" noise during their coughing fits.

A recent survey by the Washington State Department of Health suggests that primary care providers, including internists, pediatricians, and family practitioners, have a generally poor knowledge of pertussis. This monograph is intended to improve health care provider knowledge of pertussis in an effort to combat the recent rise in reported cases.

Biology

Bordetella pertussis is a coccobacillus first isolated in 1906 and named for one of its co-discoverers, Bordet and Gengou.

This organism is composed of several protein products including pertussis toxin (PT) and filamentous hemagglutinin (FHA). PT (i.e., lymphocytosis-promoting factor or pertussigen) promotes lymphocytosis, a clue to the diagnosis of pertussis in children. Both PT and FHA may mediate attachment of the organism to respiratory epithelial cells, and antibodies to these proteins appear to promote immunity. These proteins are particularly relevant to vaccine development because an acellular vaccine containing both PT and FHA has been demonstrated to be more effective at preventing clinical disease than a vaccine containing PT alone. Agglutinogens, which are produced by the organism, and an outer membrane protein (pertactin) have also been used in acellular vaccine preparations.

Transmission

Pertussis is highly contagious. Transmission occurs via respiratory secretions. Most susceptible household contacts of infected persons develop pertussis. Symptomatic adults are the primary reservoir for transmission to children (see **Pertussis in Adults**). Many adults and some children develop mild symptoms making recognition of the disease difficult and potentially facilitating transmission because of lack of treatment among unrecognized cases. Prompt diagnosis and treatment of persons infected with pertussis and chemoprophylaxis for their close contacts can reduce transmission. A carrier state (i.e., an apparently healthy person who is infected with the organism and may transmit it to others) has not been demonstrated to occur with any significant frequency and its epidemiologic importance remains controversial.

Clinical Characteristics

The incubation period for pertussis is usually 7–13 days, although it can range from 6 days to >3 weeks. The illness is composed of three phases:

1. Catarrhal phase. Early symptoms include nasal congestion, tearing, mild conjunctival injection, malaise, and low grade fever. An initially mild and nonproductive cough develops. The catarrhal phase lasts a few days to 2 weeks but can be abbreviated in a previously vaccinated adult. This stage resembles, and is often confused with, the common cold. However, many *B. pertussis* organisms are shed in the nasal secretions produced in this phase.

2. Paroxysmal phase. The cough increases in severity. A series of short expiratory bursts are often followed by an inspiratory gasp against a partially closed glottis, producing the typical whoop. Severe coughing paroxysms may cause respiratory distress, cyanosis, or post-tussive vomiting. The paroxysmal phase may last 1–2 months.

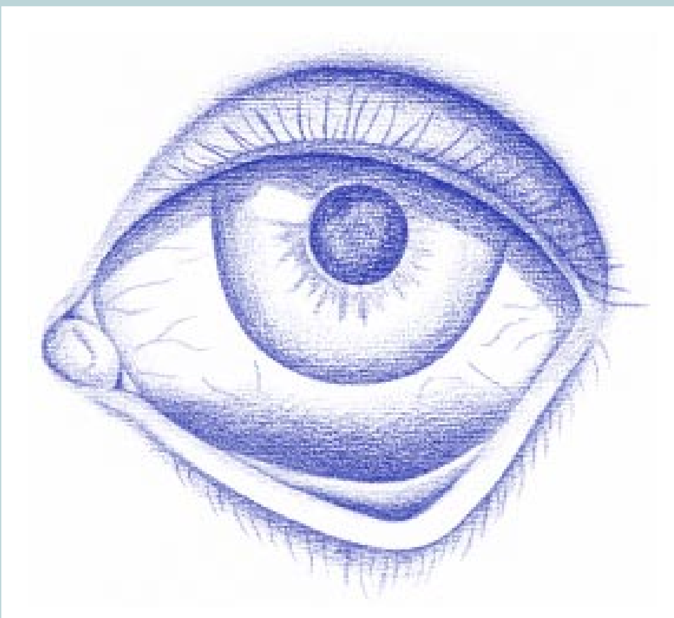

Figure 5

Subconjunctival hemorrhage may be seen as a consequence of venous engorgement of the head and neck during the paroxysmal phase of pertussis.

3. Convalescent phase. Cough intensity and frequency of the paroxysms gradually decrease. Residual coughing may persist as long as 6 months. Pertussis has been appropriately described as "the cough of a hundred days."

Atypical forms of pertussis can occur. Young infants frequently experience severe disease with apneic spells but without whooping episodes or lymphocytosis. Disease in adults may be limited to nonspecific symptoms including nasal congestion, a sore throat, and a persistent cough (see **Pertussis in Adults**). Data from several studies have indicated that one-fourth of young adults with a persisting cough have serologic evidence of pertussis infection. Because the symptoms of pertussis vary, maintaining a high index of suspicion in patients of any age who have a prolonged cough illness is important.

Clinical laboratory findings of blood specimens from persons who have pertussis often include a marked leukocytosis with total white blood cell counts occasionally >50,000 cells/mm^3 and a relative lymphocytosis of T and B cells. Neutrophils are also increased but to a lesser degree. Perihilar infiltrates or pneumonia may be found on chest x-ray. Purulent pleural effusions are rare, however a small clear effusion may be found.

Complications

The most common complications of pertussis are secondary bacterial infections, including otitis media and pneumonia. Overall, such complications develop in approximately 3% of persons who have pertussis; the highest rates occur in young infants.

Severe coughing may result in conjunctival and scleral hemorrhages (Figure 5), facial and truncal petechiae, epistaxis, central nervous system hemorrhages, subcutaneous emphysema, pneumothorax, umbilical and inguinal hernias, and rectal prolapse. Ulceration of the frenulum has also been reported (Figure 6).

Seizures and encephalopathy can occur with pertussis, most typically in infants <1 year of age. Infants are also susceptible to dehydration following protracted vomiting, and cranial nerve abnormalities have been reported.

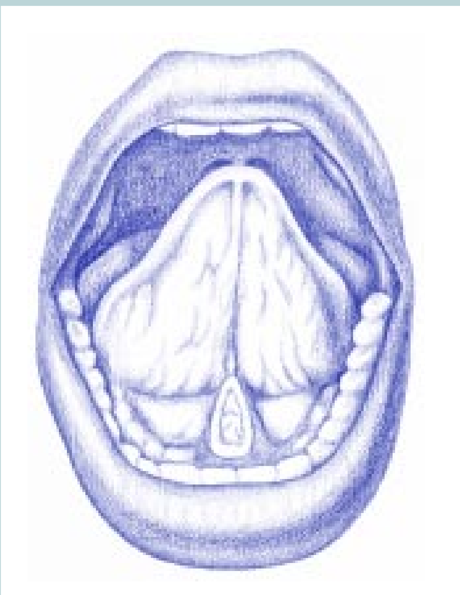

Figure 6

Ulceration of the frenulum may be seen in patients with pertussis.

In the United States during 1983–1992, at least 52 deaths were attributed to pertussis among 34,325 persons infected with this disease compared with 7,000 deaths among 265,000 infected persons in 1934 alone. Deaths resulting from pertussis are primarily limited to infants. Currently, the case fatality rate for pertussis is estimated at 6 per 1,000 for infants <1 year of age and 13 per 1,000 for those <1 month of age.

Diagnosis

Early diagnosis is an important component in the control and prevention of *B. pertussis* infection. Presently, a combination of the DFA procedure and culture is the most sensitive and specific method of diagnosis for *B. pertussis*. Approximately 50%–80% of cases of pertussis are detected by such techniques. Isolation of *B. pertussis* by culture is considered the "gold standard." The highest rate of recovery of organisms (nearly 100%) occurs in the first 2 weeks of the illness (catarrhal or early paroxysmal stages). Thereafter, the isolation of *B. pertussis* becomes difficult. Although the organism has been isolated as late as 6–7 weeks after onset, this is very unusual. Factors that may contribute to a falsely negative culture include the patient receiving antibiotics prior to collection of the specimen, poor technique used in collecting the specimen, incorrect choice of transport media, and a laboratory with staff who are unfamiliar with how to grow fastidious bacteria. A negative culture does not rule out pertussis.

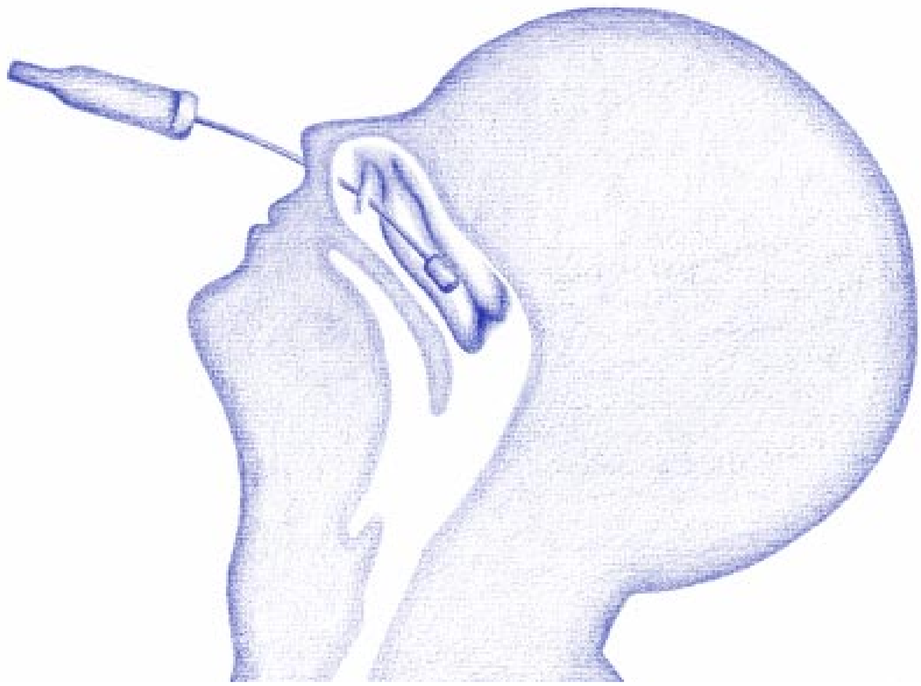

Figure 7

How to collect specimens for DFA and culture of pertussis.

To collect specimens for DFA and culture, a calcium alginate- or dacron-tipped swab is inserted through the nostril into the nasopharynx and gently rotated, ideally for 15 seconds to one minute. Avoid using cotton swabs that inhibit the growth of the organism. The nasopharyngeal swab is streaked onto the surface of the transport media (charcoal/Jones-Kendrick, or Reagan-Lowe). Streaking should be performed immediately because *B. pertussis* organisms are susceptible to drying. The swab should be left on the surface of the media while the protruding portion of the swab shaft is cut off. The wire should not be bent into the tube as skin flora may be introduced. Label the tube with the patient's name and complete a lab history form. Mail or transport the specimen and history form in a double mailing container immediately to the laboratory. If transport times exceed one day, incubate transport media at 35˚C for two days before sending. An additional specimen from the nasopharynx is streaked onto two glass slides for the DFA assay. These slides should be labelled with the patient's name and left out to air-dry. Afterwards, the slides and completed lab history form should be placed in a protective holder to prevent breakage and mailed to an appropriate laboratory (e.g., the Washington State Department of Health Public Health Laboratories or the Seattle-King County Department of Public Health laboratory) for testing.

Specimen collection for DFA and culture from patients suspected of having pertussis requires a nasopharyngeal swab of nasal secretions (Figure 7). Whereas this procedure may be uncomfortable for and difficult to perform on uncooperative young children, it gives the highest yield of organism. Nasal aspirates are also acceptable if collected early in the infection. Throat swabs are not acceptable for evaluation of pertussis. Collection kits (i.e., instructions, transport media, nasopharyngeal swabs, slides, lab history forms and mailers) and additional information can be obtained from the Washington State Department of Health Public Health Laboratories (206-361-2878 or 206-361-2865).

A variety of serological tests including agglutination, complement fixation, and indirect hemagglutination have been utilized in research labs to confirm *B. pertussis* infection. However, results from these tests are difficult to evaluate because of the heterogeneous antibody response that *B. pertussis* stimulates and the absence of a highly specific and sensitive single serologic test. Newer serologic assays (e.g., the enzyme immunoassay for IgG antibody to pertussis toxin and IgA antibody to filamentous hemagglutinin) are potential methods of diagnosis. Polymerase chain reaction (PCR)–a rapid, sensitive, and specific test–can detect *B. pertussis* organisms in asymptomatic, mildly symptomatic, or previously vaccinated persons; PCR can likely detect infection in persons treated with antibiotics. PCR has tremendous diagnostic potential but presently is still being developed.

Treatment

Some studies indicate that antibiotic treatment of pertussis (preferably with erythromycin) reduces severity of illness and frequency of death. Erythromycin is administered for 14 days at a dose of 40–50 mg/kg/day (up to a maximum of 2 g/day) in four doses. Trimethoprim-sulfamethoxazole can also be used for treatment (children: trimethoprim 8 mg/kg/day, sulfamethoxazole 40 mg/kg/day; adults: trimethoprim 320 mg/day, sulfamethoxazole 1,600 mg/day) in two doses, also given for a 14-day course. Reports exist concerning successful use of the marcrolide drugs clarithromycin and azithromycin for pertussis treatment. They appear to be

Ways health care providers may improve diagnostic yield of pertussis.

1. **Perform DFA with culture within the first 2 weeks of infection.**
2. **Perform culture before the patient receives antibiotics.**
3. **Carefully collect the nasopharyngeal specimen using a calcium alginate- or dacron-tipped swab.**
4. **Use Reagan-Lowe transport media for laboratory transport.**
5. **Utilize a laboratory experienced with growing fastidious bacteria.**

as effective as erythromycin, are much better tolerated, and will probably require a shorter duration of treatment. However, azithromycin and clarithromycin are much more expensive than erythromycin.

Persons who have suspected and confirmed cases of pertussis should maintain respiratory isolation until 5 days of an antibiotic course have been completed. Specifically, such persons should not have contact with unvaccinated children. Household and other close contacts, particularly young children, should receive medical evaluation for possible antibiotic prophylaxis to limit the spread of disease.

Hospitalization should be considered for infants <6 months of age who develop respiratory distress, feed poorly, or become lethargic. Corticosteroids may also be appropriate for infants with life threatening disease. In general, cough suppressants and antihistamines are of no proven benefit.

Epidemiology

Pertussis is transmitted from person to person through close personal contact. In the United States, vaccination has reduced the incidence of pertussis but has also resulted in a reduction in the average age of infected persons. In the prevaccine era, pertussis was primarily an illness of children 1–4 years of age. By the 1980s, >50% of cases in the United States occurred in infants <1 year of age.

Higher morbidity and mortality have been reported for persons who have crowded living conditions or low socioeconomic status. Although females have been reported to have higher pertussis-associated incidence, morbidity, and mortality, this finding is not universal.

In the United States, pertussis rates declined during 1965–1975. Beginning in 1981, rates began to increase, likely because:

a) vaccinated persons had no long-term immunity

b) many vaccine-associated side effects and reactions were reported, thus discouraging persons from receiving vaccine.

In Washington state, six pertussis-associated deaths occurred in the 1980s and an additional death occurred in 1996. The lowest pertussis rates in the state occurred in 1979 (rate: 0.3 per 100,000 cases), but the number of reported cases has increased since then with 140 cases in 1994 (rate: 3 per 100,000 cases) and 491 cases in 1995 (rate: 9 per 100,000). In 1996, 820 cases were reported (rate: 14.9 per 100,000). These rates are believed to underestimate substantially the actual numbers because pertussis is a common endemic infection in the United States that is underrecognized by both patients and health care providers.

Pertussis in adults

Pertussis in an adult may present as a mild cough illness
OR as a severe classical illness.

Pertussis is too often overlooked in the differential diagnosis of illnesses in adults that are characterized by cough. This bias against considering pertussis as a diagnosis is often based on the false assumption that pertussis does not cause illness in adults, and it may lead to substantial underdiagnosis.

The following factors contribute to the underreporting of disease in adults:

a) adults who have minor symptoms may not seek medical care

b) cultures obtained late in the course of illness may be negative

c) many health care providers who care for adults are neither familiar with the disease nor know when to report it to the local health department.

Adults are a reservoir for pertussis in the United States and often transmit the disease to children during child care. Prior to the availability of pertussis vaccine, most adults developed pertussis as children. The resultant natural immunity appears to be longer lasting than vaccine-induced immunity. Re-exposure as adults may boost immunity further and lead to milder (often unrecognized) disease. However, many adults who were vaccinated with pertussis vaccine as children have vaccine-induced immunity that lasts no more than 10–12 years, does not appear to be as complete as natural immunity, and results in more susceptibility to the disease. In 1987, an estimated 50 million adults in the United States were susceptible to pertussis; this number has probably increased.

Pertussis in an adult may present as a mild cough illness or as a severe classical illness with inspiratory whoop, post-tussive vomiting and/or paroxysms of coughing. At least two investigations have demonstrated serologic evidence of recent pertussis infection in a substantial percentage (20%–26%) of adults who have a cough illness. Thus, patients presenting with bronchitis (a common outpatient diagnosis) with a nonproductive cough may be more accurately diagnosed if they are evaluated for pertussis. Patients infected with the human immunodeficiency virus may have prolonged pertussis-associated symptoms.

Of great public health importance is the role adults may play as a reservoir of infection that can be transmitted to susceptible children. It cannot be emphasized enough that while pertussis may cause a relatively mild illness in the adult, the disease can be lethal for small infants.

Vaccines

Background

Dose	Age	Customary Age/Interval	Product*†§
Primary 1	2 months	Age ≥6 weeks	DTaP
Primary 2	4 months	4-8 weeks after 1st dose¶	DTaP
Primary 3	6 months	4-8 weeks after 2nd dose¶	DTaP
1st Booster	15-18 months**	6-12 weeks after 3rd dose¶	DTaP††
2nd Booster	Age 4-6 years before entering kindergarten or elementary school (not necessary if 4th dose [1st booster] is administered after 4th birthday)		DTaP
Additional Booster	Every 10 years after last dose		Td§§

Table 3

Routine diphtheria, tetanus, and pertussis vaccination schedule for children <7 years–United States, 1997

* Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP); diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP) is an acceptable alternative to DTaP for any of the 5 doses.

† Use diphtheria and tetanus toxoids, adsorbed (DT) if encephalopathy has occurred after administration of a previous dose of pertussis-containing vaccine. If the child is age ≥1 year at the time the 1st dose of DT is administered, a 3rd dose administered 6-12 months after the 2nd dose completes primary vaccination with DT.

§ Whenever possible, the same DTaP product should be used for all doses. If the same product is not available, Tripedia®, ACEL-IMUNE®, and Infanrix™ can be used interchangeably.

¶ Prolonging the interval does not require restarting the series.

** If the interval between the 3rd and 4th doses is ≥6 months and the child is not likely to return for a visit at the recommended age, the 4th dose of either DTaP or DTP may be administered as early as age 12 months.

†† TriHIBit™ can be administered as the 4th dose following a primary series with either DTaP or whole-cell DTP and a primary series with any *Haemophilus influenzae* type b conjugate vaccine.

§§ Tetanus-diphtheria toxoids absorbed (Td) (for adult use).

MMWR 1997; Vol. 46 / No. RR-7 p. 17

Before the development of pertussis vaccines, transmission of pertussis was prevented by isolating the patient. Quarantine regulations varied, but usually 4–6 weeks of isolation were required. The 1940 textbook, Holt's Diseases of Infancy and Childhood, stated that, "Members of the household for whom pertussis would be dangerous should be sent away."

After World War II, pertussis immunoglobulin was used for both prophylaxis and treatment. This method of passive immunization was available until 1980, when production of pertussis immunoglobulin was discontinued because controlled studies failed to demonstrate efficacy. Data from a recent study demonstrated that modern, high-dose pertussis immunoglobulin preparations (containing antibodies produced in response to immunization with acellular pertussis vaccines containing PT or PT and FHA) have a beneficial effect if administered within 7 days of disease onset.

Whole Cell Vaccines

Whole pertussis vaccines were developed in the 1930s and 1940s. Since 1947, the combination of diphtheria and tetanus toxoids with pertussis vaccine adsorbed, has been used for the immunization of infants and children in the United States. The pertussis component is made from a suspension of whole-cell pertussis bacteria inactivated by various methods depending on the manufacturer. The combined vaccines are adsorbed on to an aluminum salt to enhance immunogenicity and decrease reactivity. Estimates of vaccine efficacy vary from approximately 70%–90%.

The Advisory Committee on Immunization Practices calls for five doses of pertussis vaccine administered as DTP before age 7 years (Table 3). The vaccine is administered intramuscularly. Pertussis vaccine is ordinarily not administered to adults or children after their seventh birthday, because the severity of disease decreases with age–resulting in a higher risk-benefit ratio. A monovalent whole-cell pertussis vaccine has been used by some experts for control of outbreaks involving health care or child care personnel or as an adjunct to antibiotic prophylaxis for exposed adults at high risk of complicated disease, (e.g., chronic pulmonary disease).

The recommendation for universal vaccination of infants with DTP largely accounts for the substantial decline in the incidence of pertussis in the United States. The cessation of routine pertussis immunization in Germany, Japan, Sweden, and the United Kingdom resulted in a resurgence of epidemic pertussis in each of these countries (Figure 8).

Pertussis vaccine protects against disease and lessens disease severity in persons who do become ill. However, the vaccine provides less protection against mild disease. Partial immunization provides some protection. Neither the pertussis disease nor pertussis vaccine induces lifelong immunity. The duration of immunity following both disease and vaccination is not clearly established and, in most persons, is probably <10 years.

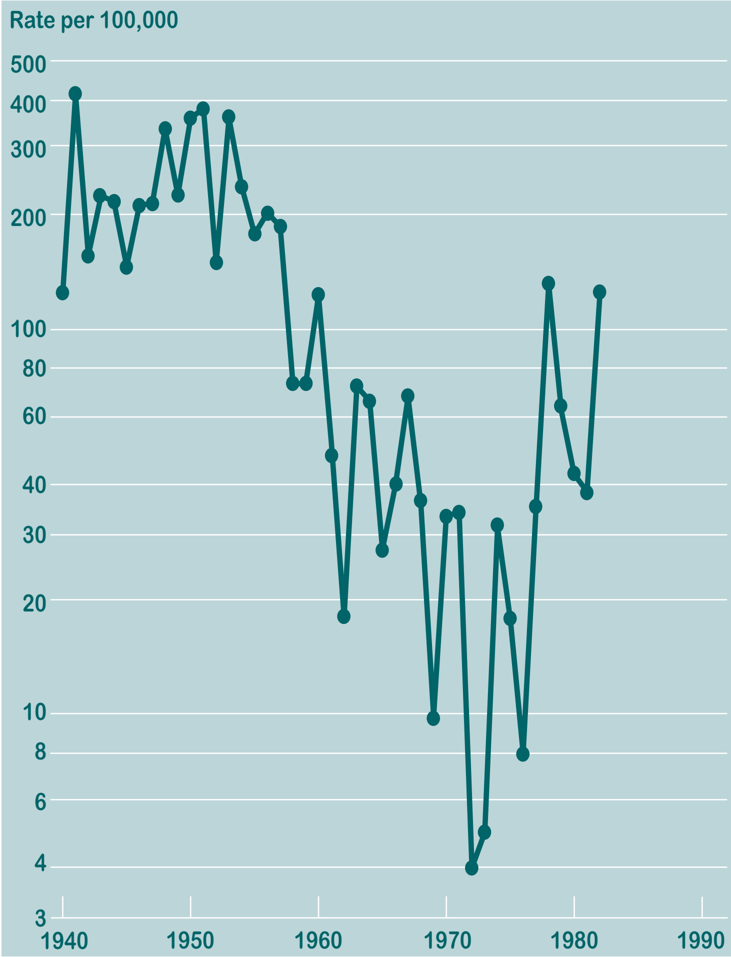

Figure 8

Pertussis attack rate by year in England and Wales, 1940–1982. The resurgence of pertussis, after the cessation of routine pertussis vaccination, is dramatic (from Cherry JD, Baraff LJ, Hewlett E. West J Med 1989 Mar; 150:319-328).

Side Effects and Adverse Reactions following DTP Vaccination

Reactions to DTP vaccination are common. One-third to one-half of children experience local swelling, redness, pain, and fever within several hours of receiving DTP. These common reactions are self-limited, without sequelae, and their incidence can be decreased by administering acetaminophen in appropriate doses at the time of vaccination and at 4 and 8 hours afterwards. The incidence of such reactions increases with age and the number of prior doses. These reactions are more likely to occur after subsequent DTP doses in children who have experienced such reactions than in those who have not. High fever (105.0˚F or 40.5˚C) and prolonged, inconsolable, unusual crying occur less often but are also without sequelae (Table 4).

Categories	Rate (%) per Dose
Redness at site	37.4
Redness >2.4cm in diameter	7.2
Swelling at site	40.4
Swelling >2.4cm in diameter	8.9
Pain at site	51
Fever ≥38˚C (100.4˚F)	47
Fever ≥40.5˚C (104.9˚F)	0.3
Drowsiness	32
Fretfulness	53
Anorexia	21
Vomiting	6
Persistent crying, for 3 to 21 h	1
High-pitched, unusual cry	0.1
Convulsion	0.06
Collapse with shock-like state	0.06

Table 4

Adverse events occurring within 48 hours of DTP vaccination.*

*These data are derived from 15,752 DTP vaccinations (modified from Cody CL, Baraff LJ, Cherry JD, Marcy SM, Manclark CR. Nature and rates of adverse reactions associated with DTP and DT immunizations in infants and children. Pediatrics. 1981;68:650-660).

Self-limited, brief, generalized convulsions, often associated with fever, occur within 24–48 hours of DTP administration after 1 per 1,750 doses of vaccine. The characteristics of such seizures resemble simple febrile convulsions and are not associated with recurrent afebrile seizures (epilepsy) or other neurologic sequelae. Data from some studies suggest that DTP may increase the rate for febrile seizures in the days immediately following vaccination. Episodes of collapse (i.e., hypotonic-hyporesponsive episodes) occur following DTP at a similar rate as self-limited convulsions. Such episodes are also without known sequelae.

The occurrence of any adverse event in temporal relation to the administration of DTP or other vaccines raises understandable concern but does not, by itself, establish that the event was caused by the vaccine. A series of studies has established that neither Sudden Infant Death Syndrome (SIDS) nor infantile spasms are caused by DTP. A temporal relation exists between the vaccine and these conditions because DTP is usually administered at the ages at which these conditions most frequently occur.

Despite a half-century of study, the concern that DTP might rarely cause acute encephalopathy that could result in permanent brain damage or death has not been resolved. In 1991, after a methodologically rigorous review of the available evidence, including studies performed in Oregon and Washington state, the Institute of Medicine concluded that while there was "insufficient evidence to indicate a causal relation between DTP vaccine and permanent neurologic damage," controlled studies were "consistent with a causal relation between DTP and acute encephalopathy" (defined as encephalopathy, encephalitis or encephalomyelitis). The Institute estimated the excess risk following vaccination with DTP to be between zero and 10.5 per million vaccinations.

Contraindications and Precautions to Pertussis Vaccination

Adverse events following pertussis vaccination that contraindicate further administration of any pertussis-containing vaccine (whole cell or acellular), include:

a) an immediate anaphylactic reaction

b) encephalopathy occurring within 7 days following DTP vaccination (defined as a major alteration in consciousness, unresponsiveness, or generalized or focal seizures that persist for more than a few hours, with failure to recover within 24 hours).

The occurrence of other adverse events following pertussis vaccination warrants careful review before additional doses of any pertussis-containing vaccine (whole cell or acellular) are administered (Table 5). These events were once regarded as contraindications but are now deemed warnings because in certain circumstances the potential benefits outweigh the risks (e.g., when the incidence of pertussis is high).

If a decision is made to defer pertussis vaccination pending further clarification of a child's neurologic status, diphtheria and tetanus vaccination should also be deferred (but not other vaccinations) because the risk for acquiring these diseases in children <1 year of age is remote in the United States. The decision to administer DTP or DT should be made by the time of a child's first birthday. Reducing or dividing doses of DTP is not recommended in any circumstance. For detailed recommendations concerning vaccination of children who have previously had convulsions or have

Contraindications to further administration of any pertussis-containing vaccine include:

a) immediate anaphylactic reaction

b) encephalopathy occurring within 7 days following DTP vaccination

Adverse event

A convulsion with or without fever occurring within 3 days of vaccination with DTP or DTaP.

Persistent, severe, inconsolable screaming or crying for $\geq$3 hours within 48 hours of vaccine administration.
Collapse or shock-like state (i.e., hypo-tonic-hyporesponsive episode) within 48 hours of vaccine administration.
Temperature of 105°F (40.5°C) or higher, unexplained by another cause, within 48 hours of vaccine administration.

Table 5

Adverse events following pertussis immunization which warrant careful review before administering additional doses of vaccine. These are warnings, not contraindications.

underlying neurologic disorders, see the recommendations of the Advisory Committee on Immunization Practices or the Report of the Committee on Infectious Diseases of the American Academy of Pediatrics (The Red Book).

Any unexpected adverse event occurring after any vaccination, especially an event severe enough to require medical attention, should be reported to the Vaccine Adverse Event Reporting System (VAERS) 1-800-822-7967. Reports can be made by persons who are not health care workers. Because a temporal association is not evidence of causation, reporting an adverse event does not denote that the adverse event was caused by the vaccine.

Acellular Pertussis Vaccines

Pertussis vaccines formulated from immunogens derived from *B. pertussis* organisms are called acellular vaccines. The principal immunogens contained in acellular pertussis vaccines include: pertussis toxin (PT–formerly called lymphocytosis promoting factor); filamentous hemagglutinin (FHA); pertactin (PRN), a 69-kd outer membrane protein; and fimbrial proteins (FIM–sometimes termed agglutinogens). Acellular pertussis vaccines containing one, two, three or four components have shown efficacy comparable to whole cell vaccines in various studies. At this time, no simple relationship exists between the number and amount of each component and a vaccine's efficacy in preventing disease. In general, acellular vaccines are immunogenic, inducing antibody to each component of the vaccine.

Acellular pertussis vaccines were licensed in Japan in 1981 for routine vaccination of children 2 years of age and beginning in 1988, at 3 months of age. Acellular vaccines are associated with lower rates of local reactions (e.g., redness, swelling, and pain), and lower rates of fever, drowsiness and anorexia than are whole pertussis vaccines. Because the incidence of fever is reduced, fewer post-immunization seizures are expected after the administration of acellular vaccines. It is not known whether rare, more serious adverse neurologic events occur less frequently following administration of acellular pertussis vaccine versus following whole pertussis vaccine.

In 1991, the first acellular pertussis vaccine–a four-component vaccine combined with diphtheria and tetanus toxoids (DTaP)–was licensed for use in the United States. In 1992, a second, two-component acellular vaccine was licensed. Because limited data existed relative to the efficacy and safety of acellular vaccines for the primary vaccination of infants, these acellular vaccines were licensed in the United States only for use as doses four and five in children 15 months to 7 years of age.

In late 1995, after obtaining results from several vaccine trials, vaccine manufacturers submitted license applications to the U.S. Food and Drug Administration for acellular pertussis vaccines for use in primary vaccination of infants and children in combination with diphtheria and tetanus toxoids (DTaP). In July 1996, the first acellular pertussis vaccine was licensed for use in infants in the United States. Additional acellular vaccines are likely to be licensed in the next two years. Manufacturers are now studying DTaP combined with other vaccines (e.g., hepatitis B [HB], *Hemophilus influenzae* b conjugated vaccines [Hib], and inactivated poliovirus [IPV] vaccines).

Because recent epidemiologic studies have established that pertussis infection in adults is common and that adults are often the source of transmission of infection to infants, use of acellular pertussis vaccine in adults is also being studied. Acellular vaccines are highly effective in preventing severe disease and moderately effective in preventing mild disease. However, no acellular vaccine has been approved for use in persons >7 years of age. Whether widespread use of acellular vaccines in adults would reduce pertussis infection rates is unknown.

Antibiotic Prophylaxis

Prompt treatment of persons infected with pertussis through the use of antibiotics limits infectivity and thus secondary spread. Because persons who have mild illness that may not be recognized as pertussis can spread the disease, prophylaxis consisting of a 14-day course of oral erythromycin is recommended for all close contacts of infected persons regardless of age and vaccine status (trimethoprim-sulfamethoxazole may be used in persons who cannot tolerate erythromycin, but its efficacy is uncertain). In 1995, an erythromycin-resistant *B. pertussis* was isolated in Arizona; its significance has not yet been established.

Bordetella parapertussis and other similar illnesses

A differential diagnosis exists for all infectious diseases. When evaluating a patient who has a prolonged cough illness, several other infectious pathogens should also be considered. These include *Bordetella parapertussis*, *Mycoplasma pneumoniae*, *Chlamydia* species, adenoviruses, and respiratory syncytial virus (RSV). *B. parapertussis* is an antigenically unique species of *Bordetella*, but clinically this organism causes a whooping cough illness. Often the illness is milder than that caused by *B. pertussis*, however fatalities have been reported. *M. pneumoniae* may cause an illness characterized by prolonged and debilitating cough. Infants can also have paroxysms of coughing from infection with *Chlamydia trachomatis*. *C. pneumoniae* can also cause a cough illness that can persist for weeks or months. Fortunately, *B. pertussis*, *B. parapertussis*, *M. pneumoniae*, and *Chlamydia* species are all susceptible to erythromycin. Although mistaking a case of pertussis for the aforementioned bacterial-induced diseases may still result in treatment with erythromycin, antibiotic prophylaxis would not be offered to the contacts of the infected patient, which could allow for further transmission of pertussis. Although a causal relationship has not been established, adenoviruses have been isolated from patients with a “whooping” cough illness. Cough may be the most prominent symptom of RSV infection. Whereas RSV infection may be paroxysmal and post-tussive, it does not cause the “whoop” that is characteristic of pertussis. Chronic sinusitis and non-infectious diseases may also produce a chronic cough.

Differential diagnosis of pertussis includes the following infectious diseases:

Bordetella parapertussis

Mycoplasma pneumoniae

***Chlamydia* species**

Adenoviruses

Respiratory syncytial virus

CME Self-Assessment Examination

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Circle correct answer

1. Which of the following is a true statement:

a. Pertussis is highly communicable

b. Widespread use of vaccine has eliminated pertussis as a public health problem of adults

c. During the past four years, the incidence of pertussis has declined in Washington state

2. Which of the following is true about patients with pertussis:

a. Lymphopenia is common

b. Lymphocytosis is common

c. Neutropenia is common

d. Thrombocytopenia is common

3. Which of the following is a true statement:

a. Pertussis is the only vaccine-preventable disease for which there has been a general increase in incidence since the 1970s

b. Pertussis is difficult to eradicate because of the carrier state

c. Pertussis vaccine is highly effective and provides lifelong immunity

4. Which of the following is not a true statement:

a. Transmission of pertussis occurs via respiratory secretions

b. Most susceptible household contacts of infected persons develop pertussis

c. Symptomatic adults are the primary reservoir for transmission to children

d. Prophylaxis of exposed close contacts of a case of pertussis should receive ampicillin

5. Which of the following is not a true statement:

a. The incubation period for pertussis is 7–13 days

b. In the catarrhal phase, the cough increases in severity and the characteristic "whoop" is heard

c. In the paroxysmal phase, severe coughing may produce post-tussive vomiting

d. The paroxysmal phase may last 1–2 months

6. Which of the following is not a true statement:

a. The most common complication of pertussis is secondary bacterial infection, including otitis media

b. The highest rates of secondary bacterial infections occur in children ages 4–6 years

c. Severe coughing may result in conjunctival hemorrhages

d. Seizure and encephalopathy can occur with pertussis

7. Which of the following is considered the "gold standard" for diagnosis of pertussis:

a. The direct fluorescent antibody procedure

b. Bacterial culture

c. Gram stain

d. Serology

8. Which of the following is the appropriate source for obtaining a specimen to be tested for pertussis:

a. Throat

b. Nares

c. Buccal mucosa

d. Nasopharynx

9. The treatment of choice for pertussis is:

a. Erythromycin

b. Penicillin

c. Ampicillin

d. Clindamycin

10. Which of the following is not true regarding pertussis vaccines:

a. Pertussis vaccine is ordinarily not administered to adults or children after their seventh birthday due to an unacceptable risk-benefit ratio

b. Pertussis vaccine lessens disease severity in persons who do become ill with pertussis

c. The duration of immunity following vaccination is probably 30–50 years in most persons

d. Reactions to diptheria-tetanus-pertussis vaccination are common

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Circle the number on the scale to the right of each of the following questions that best characterizes your opinion.

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This monograph improved my knowledge about Pertussis.	1	2	3	4	5
The monograph is a good educational format.	1	2	3	4	5
The material is concise and clearly presented.	1	2	3	4	5
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